# Necrotizing hepatitis associated with enteric salmonellosis in an alpaca

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**Abstract —** *Salmonella typhimurium* was isolated from the feces of an alpaca suffering anorexia and weight loss. Multifocal necrotizing and suppurative hepatitis consistent with bacterial infection was found in the liver biopsies. Enteric salmonellosis may be associated with milder physical and clinicopathological changes in camelids than in other large animal species.

**Résumé — Hépatite nécrosante associée à une salmonellose entérique chez un alpaga.** *Salmonella typhimurium* a été isolé des fèces d'un alpaga souffrant d'anorexie et de perte de poids. Une hépatite multifocale nécrosante et suppurative compatible avec une infection bactérienne a été diagnostiquée à partir de biopsies hépatiques. La salmonellose entérique peut être associée à des changements clinicopathologiques et physiques plus discrets chez les camélidés que chez d'autres grandes espèces animales.

*(Traduit par les auteurs)*

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A 1-year-old, 45 kg, female alpaca (*Lama pacos*) was admitted to the College of Veterinary Medicine, Oregon State University, with a history of anorexia for 8 d and a loss of 3 kg body weight over a 21-day period. Three weeks prior to admission, the alpaca had been treated with a single dose of ivermectin (Ivomec; Merck Company, Whitehouse Station, New Jersey, USA) of unknown quantity. The breeder had reported that the alpaca was consuming small amounts of pasture and grass hay, but refused to eat grain.

On presentation, the alpaca was dull, but afebrile, with normal cardiovascular and respiratory parameters. Conjunctival membranes were assessed to be tacky. She was judged to be 5% dehydrated. On digital exploration of the rectum, poorly formed, blood-stained feces were observed. Abdominal auscultation revealed hypomotile to absent forestomach contractions, with reduced borborygmi in all 4 abdominal quadrants. Transcutaneous abdominal ultrasonography with a 5-MHz linear transducer showed minimal peritoneal fluid.

The patient was restrained in a camelid chute and sedated with butorphanol tartrate (Torbugesic; Fort Dodge Animal Health, Iowa, USA), 0.05 mg/kg, bodyweight (BW), IM. Following aseptic preparation of the cutaneous site, the right jugular vein was catheterized with a 14-gauge polypropylene catheter (Abbocath-T; Abbot Ireland, Sligo, Republic of Ireland) and blood was collected for hematological and biochemical analysis. Differential diagnoses for poorly formed feces included infectious diseases such as salmonellosis (1), clostridiosis, paratuberculosis (2), coccidiosis, and giardiasis, and non-infectious causes such as feed change, excessive consumption of lush pasture or grain (3), parasitism (4), gastric ulceration, and poisoning due to arsenic or lead (4). Feces were collected and submitted for fecal flotation, aerobic and anaerobic culture, examination for *Cryptosporidium* spp., and fluorescent antibody examination for *Giardia* spp. Initial venous gas analysis revealed hyperglycemia (glucose 10.99 mmol/L; reference range, 4.94 to 7.32 mmol/L), a normal packed cell volume (41%; reference range, 26% to 42%), and total protein (58 g/L; reference range, 53 to 73 g/L). Serum chemical analysis revealed increased aspartate aminotransferase (AST) (637 IU/L; reference range, 127 to 298 IU/L) and gamma glutamyl transferase (GGT) (62 IU/L; reference range, 10 to 37 IU/L), and low blood urea nitrogen (3.6 mmol/L; reference range, 7.2 to 10.7 mmol/L). Differential diagnoses for depression and weakness included sepsis (1), hepatic lipidosis (5), neoplasia (6), gastric ulceration, and peritonitis (7).

To replace fluid deficit and provide for ongoing losses and maintenance requirements, polyionic isotonic fluid (Normosol-R; Abbot Laboratories, North Chicago, Illinois, USA), with 2 g/kg amino acids (2% solution) (Aminosyn; Abbot Laboratories) and 0.2% vitamin B complex (Vitamin B Complex; Durvet, Blue Springs, Missouri, USA) added, was administered, IV, at a rate of 105 mL/h for the first 12 h. Ceftiofur sodium (Naxcel; Pharmacia & Upjohn, Kalamazoo, Michigan, USA), 4.4 mg/kg BW, IV, q12h, was administered for broad-spectrum antibiotic coverage, sucralfate (Sucralfate; TEVA Pharmaceuticals USA, Sellersville, Pennsylvania, USA), 20 mg/kg BW, PO, q6h, for possible gastrointestinal ulceration, and flunixin meglumine (FluMeglumine; Phoenix Scientific, St Joseph, Missouri, USA), 1.1 mg/kg BW, IV, q24h, for antiinflammatory effects. On day 2, a complete blood cell (CBC) count and serum biochemical analysis revealed toxic leukocyte morphology, mild leukocytosis ($21.9 \times 10^9$ cells/L; reference range, 8 to $21.4 \times 10^9$ cells/L), band neutrophilia ($1.3 \times 10^9$ cells/L; reference range, $< 0.15 \times 10^9$ cells/L), hypoproteinemia (protein 41 g/L; reference range, 51 to 69 g/L),

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hypoalbuminemia (albumia 24 g/L; reference range, 35 to 49 g/L), hyperglycemia (glucose 8.6 mmol/L; reference range), hypertriglyceridemia (triglycerides 5.42 mmol/L; reference range), high GGT (43 IU/L) and AST (548 IU/L), high β-hydroxybutyrate (0.28 mmol/L; reference range, 0.0007 to 0.0115 mmol/L), high nonesterified fatty acids (NEFA) (1.48 mmol/L; reference range, < 0.24 mmol/L), and bile acids (584 μmol/L; reference range, < 45 μmol/L). These findings were consistent with hepatopathy and mobilization of fat reserves.

The alpaca ate small amounts of alfalfa and seemed brighter later on day 2. Fluid administration was changed to 105-mL boluses, q4h. To decrease mobilization of fat reserves, insulin (Humulin-R:U-500; Eli Lilly, Indiana, USA), 0.32 U/kg BW, SC, q24h, and dextrose (Dextrose-50%; Durvet, Blue Springs, Montana, USA), 10 g, IV, q24h, were administered. Fecal flotation also revealed 75 strongyle, 25 *Capillaria* spp., and 25 *Nematodirus* spp. ova per gram. The alpaca was subsequently treated once with albendazole (Albendazol; Pfizer Animal Health Inc, Pittsburgh, Pennsylvania, USA), 25 mg/kg BW, PO. No *Cryptosporidium* spp. were identified in the feces and fluorescent antibody examination for *Giardia* spp. on day 2 was negative. Fully formed feces were noticed at the end of day 2.

On day 3, a CBC count and serum biochemical analysis revealed ongoing hypoproteinemia (40 g/L) and hypoalbuminemia (21 g/L), and increased GGT (132 IU/L), AST (991 IU/L), and sortibol dehydrogenase (SDH) (32.8 IU/L; reference range, 1.5 to 15.7 IU/L). Decreased fat mobilization was supported by declining nonesterified fatty acids (0.33 mmol/L) and β-hydroxybutyrate (0.077 mmol/L). The liver was evaluated due to declining albuminemia and higher hepatocellular and hepatobiliary enzymes, despite supportive treatments. Transabdominal ultrasonography revealed a liver of normal size and echogenicity. Following sterile preparation of the skin at the 9th right intercostal space, 20 cm ventral to the thoracic dorsal spinous processes, 3 14-gauge biopsy cores were obtained from the liver by using a biopsy needle (Bard Biopty-Cut Biopsy Needle; C. R. Bard, Covington, Georgia, USA). Two liver biopsies were fixed in 10% formalin and submitted for histopathologic examination and 1 biopsy was submitted for aerobic and anaerobic culture. Serum biochemical analyses on day 4 revealed normalizing total serum protein (54 g/L) with improved hypoalbuminemia (24 g/L). Decreasing hepatobiliary damage was noted due to decreasing GGT (96 IU/L), AST (686 IU/L), SDH (5.2 IU/L), and bile acids (45.5 μmol/L). Further improved energy utilization was seen with decreased triglyceride (0.61 mmol/L), β-hydroxybutyrate (0.007 mmol/L), and nonesterified fatty acid (0.14 mmol/L) levels.

By day 5, fecal culture identified *Salmonella typhimurium,* lysine negative strain, which was sensitive to ceftiofur sodium and resistant to penicillin, tilmicosin, and erythromycin. Sucralfate was discontinued on day 5. Fluid therapy was discontinued once the alpaca regained its full appetite and water intake with normal fecal consistency. Histopathologic evaluation of the liver biopsy taken previously revealed randomly distributed foci of neutrophilic infiltrates and of liquifactive necrosis with associated neutrophils. Special stains for bacteria, fungi, and spirochetes were negative. Only mild accumulation of lipid was found in scattered hepatocytes. There was no evidence of portal inflammation, fibrosis, or bilary ductule hyperplasia. Histologic findings were consistent with bacterial embolism. Bacterial culture was negative.

A CBC count and serum biochemical analysis on day 8 showed a high white cell count ($21.2 \times 10^9$ cells/L); improved total protein (54 g/L) and hypoalbuminemia (29 g/L); and normal GGT (49 IU/L), AST (271 IU/L), and SDH (2.9 IU/L). Insulin therapy was discontinued by day 7. Ceftiofur sodium was discontinued on day 9. The alpaca was discharged on day 14, clinically normal; and 3 mo following discharge, it was maintaining weight and appetite.

Enteric salmonellosis in New World camelids has not been reported previously. The rare reports of *Salmonella* spp. infections describe septicemic salmonellosis with no apparent involvement of the gastrointestinal tract (1,4). Thus, these infections appear to be uncommon or undiagnosed. No profuse or watery diarrhea was observed at any time and fully formed feces were noticed after 24 h of admission, in contrast to the watery diarrhea seen in most cases of enteric salmonellosis treated at this clinic. Additionally, hematological and serum biochemical changes were relatively mild, compared with those of acute salmonellosis seen in horses and ruminants. Hypoproteinemia was the most striking abnormality. As hypoalbuminemia is a common finding in camelids with enteritis (8) and other illnesses, and as fecal diagnostic testing for salmonellosis in camelids is performed infrequently, enteric salmonellosis is common but remains undiagnosed in most camelids. More routine culturing, serial fecal cultures, or fecal testing with the polymerase chain reaction would be necessary to estimate the prevalence of infections

Interpretation of this case was further complicated by clinicopathologic evidence of liver disease and fat mobilization. Hepatic lipidosis and hyperlipemia due to excessive fat mobilization is associated with changes in liver enzymes, as well as the vague signs of anorexia and weight loss (5). These disorders can occur in camelids of any signalment, not only camelids with higher energy requirements as in lactation and pregnancy. Nonesterified fatty acids are more commonly increased than are blood triglycerides in camelids with disorders of energy metabolism. The causes of hyperlipemia in camelids have not been established, and may possibly relate to the inflammatory nature of this camelid's disease. The fluid treatments (9) and insulin were chosen to enhance triglyceride clearance and decrease NEFA and ketone body production, in order to limit further hepatic damage. These treatments may have been beneficial, although necrosis was a more marked feature than lipidosis in this alpaca.

Despite the negative results on tissue culture, the hepatic necrosis may have been related to the enteric infection. Multifocal suppurative necrotizing hepatitis is characteristic of bacterial septicemia, including salmonellosis (10), which can invade the liver by way of septicemia or ascending cholangiobillary infection. The antibiotic course may have inhibited growth of *Salmonella* spp. from the liver biopsy in this case.

Other treatment included antibiotics and anti inflammatory agents. Although the use of antibiotics to treat enteric salmonellosis is controversial, the active hepatitis in this alpaca supported their use. As camelids frequently develop hypoalbuminemia with gastrointestinal disease, including enteritis, fluids should either not be delivered in excess quantity or be administered with plasma. Treatment for gastrointestinal ulceration should be considered in stressed camelids suffering from hypoalbuminemia due to glandular ulcers in the 3rd compartment or possibly from ulcerative enteritis, although the efficacy of such treatment is unproven. CVJ

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